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Ethnic Cluster of HTLV-I Infection in Israel Among the Mashhadi Jewish Population

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A high prevalence of human T-lymphotropic virus type I (HTLV-I) infection among Israeli Jews was previously reported. In the present study, screening for HTLV-I of Israeli Jews was expanded to 10 ethnic groups. HTLV-I antibodies were tested by the particle agglutination assay, ELISA, and by Western blot as a confirmatory method. The HTLV-I proviral genome was tested by nested PCR with *tax* primers (SK43/SK44 and Tr101/Tr102). The PCR tests were carried out in all seropositive subjects and the seronegative family members of the seropositives subjects in the Iranian population. Sixty-eight of the 1,679 subjects (4.1%) were found to be seropositive. The Jews originating from Mashhad had the highest infection rate of 60/306 (20%). Of the 479 Iranian non-Mashhadi Jews, 6 (1.3%) were seropositive. Of the 894 non-Iranian Israelis, only 2 (0.2%) were seropositive. HTLV-I proviral DNA was found in the peripheral blood lymphocytes of 66 out of 68 seropositive subjects and 6 out of 75 seronegative subjects. Sixty out of 123 (49%) Mashhadi Jews and 8 out of 14 (57%) non-Mashhadi Iranian Jews were PCR-positive. Three out of three seropositive non-Iranian Israelis were PCR positive. One non-Iranian Israeli (who originated from Ukraine) without family connections to the Iranian Jews was also PCR-positive. One hundred eighteen saliva samples (84 from subjects of Mashhadi origin, 31 from Iranian origin, and 4 of other origins) were also screened. Antibodies for HTLV-I were found in 23 out of 46 saliva samples from the individuals with particle agglutination (PA) and/or PCR-positive findings in blood. Twenty out of 23 PA-positive saliva samples also contained the proviral DNA. It is concluded that HTLV-I infection in Israel is mainly limited to Jews originating from Iran (most of them from Mashhad) and their family members. ***J. Med. Virol. 56:269–274, 1998.*** © 1998 Wiley-Liss, Inc.

KEY WORDS: human T-lymphotropic virus type I (HTLV-I); Mashhadi Jews; blood; saliva; antibody; proviral DNA

INTRODUCTION

Human T-cell leukemia virus type I (HTLV-I) was the first human oncogenic retrovirus to be identified and isolated [Poiesz et al., 1980]. It is recognized as an etiologic agent of adult T-cell leukemia (ATL) [Hinuma et al., 1981] and HTLV-I–associated myelopathy (HAM), also known as tropical spastic paraparesis (TSP) [Gessain et al., 1985; Osame et al., 1987]. The majority of HTLV-I–infected individuals are asymptomatic carriers, and only about 0.5–4% eventually acquire malignancy or HAM/TSP [Neil and Forrest, 1987]. Clustering of HTLV-I was noted originally in a group of patients from southwestern Japan [Shioiri et al., 1993]. Additional clusters have since been documented in the United States, especially the southeastern regions, Central and South America, Africa, the Middle East, India, and some areas of the Far East outside Japan [Saxinger et al., 1984; Riedel et al., 1989; Araujo et al., 1992; Buckner et al., 1992]. In Europe, clusters of HTLV-I infections are present in countries with historical ties to the Caribbean or other regions in which HTLV-1 is endemic [Taylor, 1996].

Meytes et al. [1990] reported a high rate (11.5%) of HTLV-I infection in a group of 208 Israeli subjects who had emigrated from Mashhad, Iran. An even higher rate (23%) was noted in a later study of 83 Mashhad-born Jews [Achiron et al., 1993]. The latter group was also characterized by a high incidence of HAM/TSP morbidity. The Mashhadi Jews intermarried for gen-

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TABLE I. Antibody Profile of HTLV-I and Proviral HTLV-I DNA in Blood of Israelis of Different Origins

Place of origin	Anti–HTLV-I antibody (PA)[a] positive/total	Percent of PA-positive	Anti–HTLV-I antibody (ELISA)[b] positive/total (%)	Anti–HTLV-I antibody (WB)[b] positive/total (%)	Proviral HTLV-I DNA (PCR)[c] positive/total (%)
Mashhad	60/306	20	57/60 (95%)	60/60 (100%)	60/123 (49%)
Iran (non-Mashhad)	6/479	1.3	6/6 (100%)	6/6 (100%)	8/14 (57%)
Israelis from different origin[d]	2/894	0.2	2/2 (100%)	3/3 (100%)	4/4 (100%)
Total	68/1679	4.1	65/68 (96%)	69/69 (100%)	72/143 (50%)

[a]PA: particle agglutination assay.
[b]Only PA-positive sera were also tested by the enzyme-linked immunosorbent assay (ELISA) and by the Western blot (WB).
[c]Total 143 individuals tested by the polymerase chain reaction (PCR) included the 68 seropositives and 75 seronegative family members of the seropositives subjects and controls.
[d]The group of 894 non-Iranian Israelis included 407 Israeli native Jews, 276 Jews originated from Europe, 45 from Iraq, 54 from the republics of former Soviet Union, 67 from Morocco, 4 from Egypt, 4 from India, 1 from Japan, and 36 Israeli Arabs.

erations, thereby creating a genetically isolated and distinct community in both Mashhad (Iran) and Israel [Sidi et al., 1990; Shohat et al., 1991]. However, the source of the HTLV-I infection in Israel among the Mashhadi Jews has not yet been addressed.

In an earlier study designed to determine the origin and genetic diversity of HTLV-I in this population, selected regions of the HTLV-I *gag, pol, env,* and *pX* genes from the DNA of Mashhadi Jews were enzymatically amplified by the polymerase chain reaction (PCR) and sequenced [Nerurkar et al., 1995]. In the present study, blood and saliva samples were examined from HAM/TSP and ATL patients and healthy HTLV-I carriers from Mashhad and other Iranian cities. In addition, other Jewish ethnic groups originating from all over the world as well as subjects of third- and fourth-generation native Israelis were also studied.

MATERIALS AND METHODS

Subjects

The study population included 1,679 subjects, 786 males and 893 females aged 1.5 to 87 years; 1,643 were Israeli Jews (immigration and natives) and 36 were Israeli Muslims (196 individuals were drug addicts) (Table I). Blood samples were collected from all subjects and saliva samples from 115 Iranian Jews and 3 Jews of other origin.

Preparation of Blood and Saliva Samples

Blood samples were obtained by venipuncture. Peripheral blood mononuclear cells were separated by Ficoll-Hypaque density centrifugation and washed twice in phosphate-buffered saline (PBS). Lymphocytes were counted and 5–10 × 10^6 lymphocytes were used for DNA extraction.

Each subject was asked to gargle 10 ml of sterile 0.9% NaCl solution for 20 sec and spit the fluid into a sterile test tube. To enrich the human saliva cells, the solution was centrifuged at 2,000 rpm for 10 min, the supernatant was discarded, and the amount of cells in the pellet was counted; 5 × 10^6 cells were used for DNA extraction.

Cellfree saliva was obtained by having the subject to chew a chewing gum for over 5 min and then spit into a sterile test tube. The saliva was centrifuged at 3,000 rpm for 15 min and the supernatant was filtered. Sera and saliva samples were stored at –20°C until tested.

Antibody Detection

Initial screening for detection of anti–HTLV-I antibodies in the sera and saliva was carried out by particle agglutination (PA) test (Serodia ATLA, Fujirebio, Tokyo, Japan) [Ikeda et al., 1984]. The titer of antibody was expressed as the highest dilution of serum or saliva yielding definite agglutination. A serum or saliva dilution of 1:16 or higher was interpreted as positive. All samples that were PA-positive or "±," as well as some negative serum samples, were tested by two ELISA commerical kits (Vironostica Organon Teknika, Duham, NC or Cambridge Biotech, Worcester, MA) [Kline et al., 1991], and the presence of anti–HTLV-I antibodies was confirmed by two of three Western blot (WB) kits (Fujirebio, Tokyo, Japan; Bio-Rad Laboratories, Hercules, CA; and Cambridge Biotech) [Lal et al., 1992].

DNA Purification and PCR

Genomic DNA was extracted by the SDS/proteinase K method [Miller et al., 1988] from peripheral blood lymphocytes and cells from saliva samples. DNA was isolated by overnight incubation of samples at 37°C in lysis buffer (100 mM NaCl, 10 mM Tris-HCl, pH 8, 25 mM EDTA, and 0.5% SDS) containing 100 μg/ml proteinase K. After adding 6 M NaCl, the DNA was precipitated with ethanol and redissolved in distilled water. The readings for DNA concentration were done at 260 nm; for protein at 280 nm. The ratio 260/280 was then calculated and in all cases a value of 1.8–2.0 was detected (conversion 1 OD = 50 μg/ml). Blood and saliva samples were tested by PCR for proviral HTLV-I DNA. One μg DNA (equivalent to 10^5 cells) was amplified in a reaction mixture containing 20 mM Tris-HCl (pH 8.4), 50 mM KCl, 2 mM $MgCl_2$, 10 mM of each dNTP, 25 pmol of each primer, 1.5 μl Taq polymerase (Appligene-Oncor, France) in a total volume of 50 μl. To increase sensitivity, nested PCR was carried out. To start the PCR the *tax*-specific Tr101/Tr102 primers were used and the inner primers were SK43/SK44 [Maloney et al., 1992].

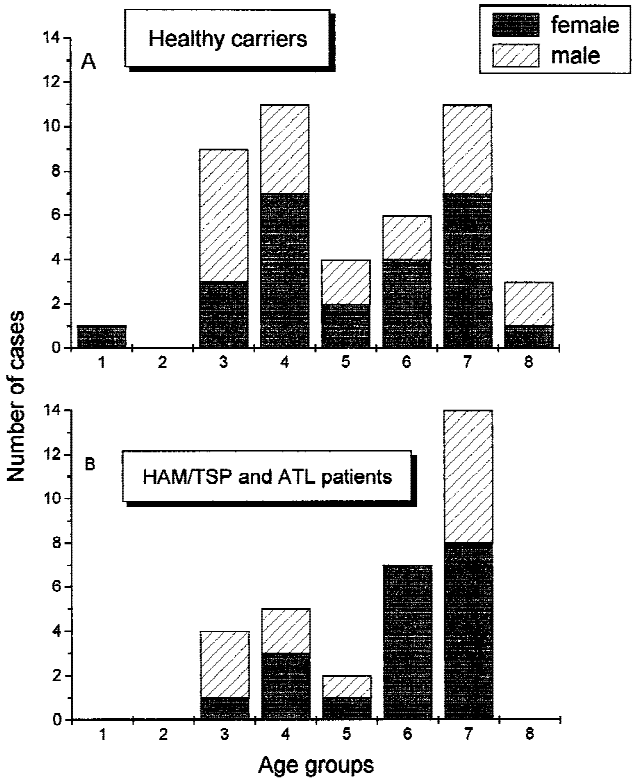

Fig. 1. Sex and age distribution in HTLV-I infected population. The group of HTLV-I–positive healthy carriers **(A)** consisted of 40 individuals; group **(B)** comprised 23 HAM/TSP and five ATL patients. The numbers designate the following age groups: 0–10 years old (1), 11–30 (2), 31–40 (3), 41–50 (4), 51–60 (5), 61–70 (6), 71–80 (7), and 81–90 (8).

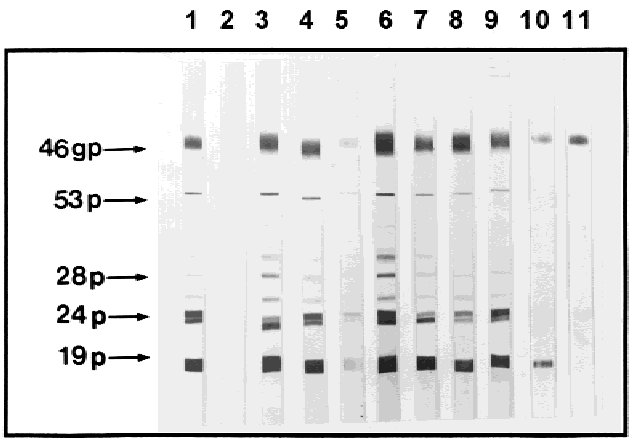

Fig. 2. Western blot of serum and saliva samples of HTLV-I healthy carriers and HAM/TSP patients of Iranian origin. The Western blot kit was from Fujirebio. Lanes 1 and 2 are positive and negative controls. Lane 5 is a weak positive serum (PA titer 1:512) and lanes 7 and 8 are strong positive sera of healthy carriers (titers by PA were 1:1024 and 1:2048, respectively). Lanes 3, 4, 6, and 9 show the antibody pattern in strong positive sera of TSP/HAM patients (titers 1:8192, 1:2048, 1:8192, and 1:2048, respectively). Lanes 10 and 11 are the antibody pattern in positive saliva samples of TSP/HAM patients with the PA titers of 1:16 and 1:64, respectively.

RESULTS

The study population contained 306 Jews from Mashhad, 129 males and 177 females aged 1.5 to 87 years. Sixty (20%) were found to be HTLV-I seropositive by particle agglutination (PA) assay, and they were also PCR-positive (Table I). Of the 479 other (non-Mashhadi) Iranian Jews, 6 (1.3%), including 2 out of 100 (2%) from Shiraz, were seropositive. The remaining 893 subjects were non-Iranian Israelis from 10 different ethnic groups; only two were seropositive and three were PCR-positive (Table I), one born in Poland, the other in India, and the third in Ukraine. One was married to a Mashhadi, the other to an Iranian HTLV-I seropositive patient, and the third had no family connections with Mashhadi or Iranian Jews. None of the non-Iranian drug addicts was seropositive.

The initial screening was undertaken by the PA test. The titer of HTLV-I antibodies ranged from 1:32 to 1:2,097,152 (mean 12,039) among the seropositive individuals. Of the total 68 HTLV-I seropositive individuals, 40 were healthy carriers, 23 Iranian had HAM/TSP, and five had ATL. The HAM/TSP patients had the highest HTLV-I titers (mean 1:8,192) of these three subgroups, in accordance with findings in other areas of the world in which HTLV-I is endemic. The mean titer for healthy HTLV-I carriers was 1:1,024, and the mean for ATL patients was 1:512. The difference between the mean values of the titer was not statistically significant ($P > 0.3$, student's t-test). Twenty-eight of the seropositive individuals were males and forty females. The women had higher HTLV-I antibody titers than males (mean 1:20,510 and 1:3,256, respectively). However, this difference was not statistically significant, because of the high variance ($P > 0.2$, student's t-test). No correlation was found between age and anti–HTLV-I antibody titer. Both patients and healthy HTLV-I carriers show the first peak of infection in adulthood (41–60) and the second peak in old age (71–80) (see Fig. 1) as tested by both PA and Western blot assays.

All PA-positive samples were tested by five additional different kits of ELISA and WB (Fig. 2). As shown in Table II, the best result were obtained by all-WB kits, with 3–4% false negatives by ELISA. The PA assay did not yield any false positive results. However, false negative result was found in 1 (1.4%) out of 69 cases tested. It is concluded that WB is the most sensitive test, and that PA was more sensitive than the ELISAs.

HTLV-I proviral DNA was sought in the peripheral blood lymphocytes of 66 out of 68 seropositive subjects and 6 out of 75 seronegative subjects. Sixty (49%) out of 123 Mashhadi Jews and 8 (57%) out of 14 non-Mashhadi Iranian Jews were PCR positive (Fig. 3). Three out of three seropositive and one seronegative female (originating from Ukraine) non-Iranian Israelis were PCR-positive.

In addition to screening for anti–HTLV-I antibodies in blood, saliva samples were also tested. Determination of anti–HTLV-I antibodies in saliva was carried out in 46 individuals with PA- and/or PCR-positive

TABLE II. Comparison of Three HTLV-I Screening Tests and Three Confirmatory Western Blot Tests in Seropositive Subjects

Tests	Sensitivity positive/total	Percent of positivity
PA (Fujirebio)	68/69	99
Elisa (Vironostica)	45/47	96
Elisa (Cambridge)	58/60	97
WB (Fujirebio)	54/54	100
WB (Bio-Rad)	58/58	100
WB (Cambridge)	4/4	100

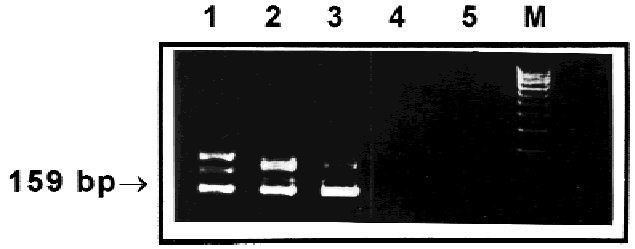

Fig. 3. Polymerase chain reaction of HTLV-I proviral DNA from peripheral blood mononuclear cells of an HTLV-I healthy carrier and an HAM/TSP patient. Lane 1 shows positive control DNA from MT-4 cells; Lane 2, an Iranian-born HAM/TSP patient; Lane 3, a Mashhadi-born HTLV-I healthy carrier; Lanes 4 and 5, water, steps 1 and 2, respectively; and Lane M1, 100 bp Ladder (MBi).

findings in blood and 72 seronegative individuals (Table III). The seropositive subgroup included 21 Iranian HAM/TSP patients, one ATL Mashhadi patient, and 24 healthy carriers. PA-positive findings were noted in the saliva of 23/46 (50%) seropositive subjects: in 59% of the HAM/TSP patients (mean of titer 1:78) and 42% of the healthy carriers (mean of titer 1:44). The difference of the titer of the HAM/TSP patients and healthy carriers was not statistically significant ($P > 0.2$, student's t-test). The single ATL patient was PA-negative. Titers of antibodies to HTLV-I were significantly lower in saliva than in blood ($P < 0.01$, student's t-test). The ELISA yielded poor results in saliva (Table III). From the 23 PA-positive saliva samples, 13 were positive by WB and 4 were WB-indeterminates, with antibodies only to *gag* (p53, p43, p24, p19) and p40 *tax* proteins (Fig. 2). Two persons who were negative for anti–HTLV-I antibodies in blood had PA-positive findings in saliva, confirmed by WB and by PCR (Table IV). The PA test was found to be the best for HTLV-I antibodies screening in saliva. WB was confirmatory for saliva in 57% of cases. Nested PCR with the *tax* pair primers SK43/SK44 and Tr101/Tr102 showed the integration of HTLV-I proviral DNA into saliva cells of all seropositive subjects (Table III).

Among the 60 seropositive Mashhadi Jews, 11 children of two families of HAM/TSP patients and four families of healthy carriers also had HTLV-I infection (see Fig. 4); all had been breast-fed. In five families, both partners were infected; in two transmission was from an infected Iranian husband to a spouse of another origin, and in the remaining three families it was from a wife of Mashhadi origin to a spouse of another origin. An additional four families in which both partners originated from Mashhad also indicated sexual transmission (Table V).

DISCUSSION

Achiron et al. [1993] and Meytes et al. [1990] reported that HTLV-I infection was endemic to Mashhadi Jews. In the present study, we increased significantly the number of subjects examined from Iran and Mashhad (total 785 individuals) and also investigated groups of Jews born in other countries (n = 894). The highest rate of HTLV-I infection (20%) was observed in the Mashhadi Jews (Table I). The results were confirmed recently by Safai et al. [1996], who found Mashhad to be an endemic area. These researchers studied HTLV-I infection in the non-Jewish population of Mashhad and found 3% incidence of HTLV-I infection. In both studies, serum for HTLV-I testing was taken in a general hospital setting. In addition, healthy volunteers and elderly subjects from a retirement home for Mashhadis were tested. The same prevalence rate of HTLV-I was noted in the 20- to 30-year and the elderly age groups.

The difference in HTLV-I seropositivity rates between the Jewish and non-Jewish Mashhadi population in Iran may be traced to historical reasons. In the 18th century, the Jews in Iran were subjected to persecution. To save their lives they overtly converted to Islam, but secretly continued to practice Judaism. In order to isolate themselves from the surrounding Muslim population, the Mashhadi Jews married only among themselves. With time, this produced a closed community with close genetic ties [Achiron et al., 1993]. It is presumed that HTLV-I was brought to Mashhad from Africa [Saxinger et al., 1984] or India [Babu et al., 1993] in the Middle Ages, when the city served as an important trade center. This, too, may have contributed to the higher rate of HTLV-I seropositivity among Mashhadi Jews, since most of them were merchants in contrast to the Muslim Mashhadi residents.

It remains unclear whether Mashhad is the only town in Iran to which HTLV-I is endemic. Our study showed HTLV-I infection also among non-Mashhadi Iranian Jews originating from Shiraz, Isfpahan, and other towns, with no relatives in Mashhad, but at a much lower rate. Safai et al. [1996] did not test Muslims beside those in Mashhad and the Muslims, in Gonbad-Kavous. Mashhadi Muslims had 3% infection and none in the latter town.

Farid et al. [1995] reported that breast-feeding is the main source of HTLV-I spread in Muslim families in Mashhad. They found a 74% transmission rate by breast-feeding in seropositive mothers with ATL or HAM/TSP (with no history of blood transfusion, intravenous drug use, or hemodialysis). Similar findings were obtained in the present study in which most of the HAM/TSP and healthy carrier families had both infected parents and infected children, and all the children had been breast-fed and none were drug addicts

TABLE III. Anti–HTLV-I Antibody and HTLV-I Proviral DNA in Saliva

Subject groups	Anti–HTLV-I antibody positive/total (%)					Proviral HTLV-I DNA positive/total (%)
	PA[a]	Range of titer	Mean of titer	ELISA	Western blot	
HAM/TSP patients	13/22 (59%)	1:16–1:256	1:78	3/13 (23%)	11[b]/13 (87%)	12/13 (92%)
HTLV-I healthy carriers	10/24 (42%)	1:16–1:128	1:44	0/10 (0%)	6[c]/10 (60%)	8/10 (80%)
Negative donors	0/72 (0%)					
Total	23/118 (19%)			3/23 (13%)	17/23 (78%)	20/23 (87%)

[a]PA: particle agglutination assay. The PA-positive saliva samples were then tested by the ELISA, Western blot (WB) and PCR.
[b]The saliva samples of HAM/TSP patients were tested by WB; nine samples were positive (antibodies to both *gag* and *env* antigens were found) and two indeterminates (either *gag* or *env*).
[c]Among the HTLV-I PA-positive healthy carriers, four were WB-positive and two indeterminates.

TABLE IV. Sexual Transmission of HTLV-I Infection in Three Mixed Families[a]

Family	Origin	Blood			Saliva		
		PA	WB	PCR	PA	WB	PCR
S. I							
Male	Iran	+	+	+	+	+	+
Female	India	+	+	+	–	–	–
S. II							
Male	Iran	+	+	+	+	+	+
Female	India	–	–	+	+	+	+
M.							
Male	Egypt	–	+	+	+	Ind	+
Female	Mashhad	+	+	+	+	+	+

[a]Particle agglutination assay, Western blot, and Polymerase chain reaction were employed to search for HTLV-I in blood and saliva. Ind designates a WB indeterminate.

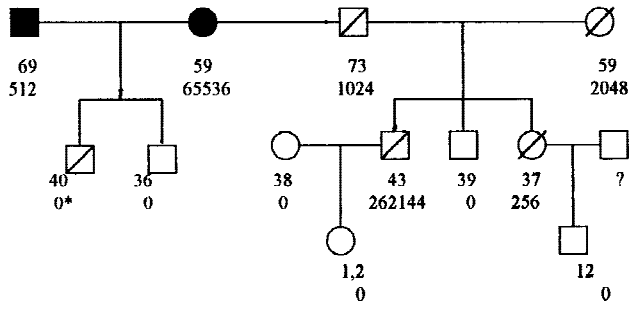

Fig. 4. Pedigree of the Mashhadi family E. □, denotes HTLV-I negative male subjects; ○, HTLV-I negative female subjects; ◪, HTLV-I positive male healthy carriers; ∅, HTLV-I positive female healthy carriers; ■, HTLV-I positive male TSP/HAM patient; and ●, HTLV-I positive female TSP/HAM patient. Numbers indicate the age (top) and the anti–HTLV-I antibody titers (bottom) of the individuals. Asterisk denotes PCR-positive.

TABLE V. Sexual Transmission of HTLV-I Infection in Mashhadi Families[a]

Family	Origin	Blood			Saliva		
		PA	WB	PCR	PA	WB	PCR
R.							
Male	Mashhad	+	+	+	+	–	ND
Female	Mashhad	+	+	+	+	Ind	+
B.							
Male	Mashhad	+	+	+	–	ND	+
Female	Mashhad	+	+	+	–	ND	+
E.							
Male	Mashhad	+	+	+	–	Ind	+
Female	Mashhad	+	+	+	+	+	–
L.							
Male	Mashhad	+	+	+	+	–	ND
Female	Mashhad	+	+	+	–	–	ND

[a]Particle agglutination assay, Western blot, and polymerase chain reaction were employed to search for HTLV-I in blood and saliva. Ind designates a WB indeterminate; ND, not determined.

or promiscuous. Another pathway of virus spread is intravenous drug use [Aboulafia et al., 1993]. Maayan et al. [1992] reported a 4% seropositivity rate among drug addicts in Israel. Nevertheless, in the present study, no HTLV-I–positive subjects was found among the 196 drug addicts of non-Iranian origin and none of the Mashhadi seropositive subjects were drug addicts. Blood transfusion was not a major route of transmission in the Iranian population. Only one HAM/TSP patient born in Iran (not Mashhad) was found to be seropositive 15 years after a transfusion, similar to the finding of Farid et al. [1995]. Our tests in other ethnic groups in Israel showed that HTLV-I infection has not spread from the Mashhadi Jews to other ethnic groups in this country. This may be due to the fact that blood donations in Israel are now screened for HTLV-I. Only one female subject from the Ukraine was infected. However, she was a newcomer to Israel and probably was infected in Ukraine.

Achiron et al. [1996] detected previously HTLV-I proviral genomic DNA by nested PCR in saliva samples of 71% of HTLV-I infected Mashhadi-born Jews. Miyoshi et al. [1992] recently detected HTLV-I proviral DNA by PCR in six saliva samples from HTLV-I asymptomatic carriers and ATL patients, and Archibald et al. [1988] noted antibodies to HTLV-I antigens by radioimmunoprecipitation assay in 22 (79%) of 28 saliva samples from seropositive (including one ATL) Japanese patients. HTLV-I antibodies have been found also in saliva samples from seropositive patients with Sjögren's syndrome [Mariette et al., 1993], and proviral HTLV-I genome was detected in the salivary and lachrymal glands of HTLV-I–infected transgenic mice [Bieberich et al., 1993].

Saliva screening in the present study disclosed antibodies for HTLV-I by PA assay in 23 of 46 saliva samples for individuals with PA- and/or PCR-positive findings in blood. Archibald et al. [1988] found a reversed ratio of the *gag*/*env* rate (45%:95%) of anti–HTLV-I antibodies in saliva of seropositive Japanese subjects. In contrast to our funding, where the ratio of *gag*/*env* was 16%:17%, Belec et al. [1996] found that the PCR-positive were always also antibody-positive in saliva samples, similar to our present findings. The

lower rate of anti–HTLV-I antibodies found by us in saliva as compared to blood can be explained by the lower virus load and the inhibitory factors found in saliva. Whole saliva also contains proteolytic enzymes, which may interfere with antibody determinations [Holmstrom et al., 1990; O'Farrel et al., 1997].

The present study was expanded to 10 ethnic groups in Israel. The presence of HTLV-I infection was found mostly only in a closed community of Iranian Jews, the majority of them from Mashhad. The proviral DNA of HTLV-I as well as antibodies to HTLV-I were detected in both blood and saliva samples of this population. Spread of infection from the Mashhadi Jews to other ethnic groups in Israel was not detected.

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REFERENCES

Aboulafia DM, Feigal E, Vranzian K, Bennett C, Blattner W, Moss A, Slamon D (1993): Human T-cell leukemia virus (HTLV-I) serodiagnostic testing: disparate results among cohort of intravenous drug users. AIDS Research and Human Retroviruses 9:1043–1050.

Achiron A, Pinhas-Hamiel O, Doll L, Djaldetti R, Chen A, Ziv I, Avni A, Frankel G, Melamed E, Shohat B (1993): Spastic paraparesis associated with HTLV-I: A clinical, serological and genomic study in Iranian-born Mashhadi Jews. Annals of Neurology 34:670–675.

Achiron A, Pinhas-Hamiel O, Barak Y, Doll L, Offen D, Djaldetti R, Frankel G, Shohat B (1996): Detection of proviral human T-cell lymphotropic virus type I DNA in mouthwash samples of HAM/TSP patients and HTLV-I carriers. Archives of Virology 41:147–153.

Araujo AWC, Ali A, Newell A, Dalgleish AG, Rudge P (1992): HTLV-I infection and neurological disease in Rio de Janeiro. Journal of Neurology, Neurosurgery and Psychiatry 55:153–155.

Archibald D, Essex M, McLane M, Sauk J, Tachibana N, Mueller N (1988): Antibodies to HTLV-I in saliva of seropositive individuals from Japan. Viral Immunology 1:241–246.

Babu PG, Gnanamuthu C, Saraswathi NK, Nerurkar VR, Yanagihara R, John TJ (1993): HTLV-I–associated myelopathy in South India. AIDS Research and Human Retroviruses 9:499–500.

Belec L, Georges AJ, Hallouin MC, Mohamed AS, Morand-Joubert L, Georges-Courbot MC (1996): HTLV-I excretion and specific antibody response in paired saliva and cervicovaginal secretions. AIDS Research and Human Retroviruses 12:157–167.

Bieberich CJ, King CM, Tinkle BT, Jay G (1993): A transgenic model of transactivation by the tax protein of HTLV-I. Virology 196:309–318.

Buckner C, Roberts C, Foung S, Lipka J, Reyes R, Hadlock K, Chan L, Gongora-Biachi R, Hjelle B, Lal R (1992): Immune responsiveness to the immunodominant recombinant envelope epitopes of HTLV-I and 2 in diverse geographic populations. Journal of Infectious Diseases 166:1160–1163.

Farid R, Poryamoth N, Godarzi A, Rafatpanah H, Amina H, de The G, Gessain A (1995): A familial sero-epidemiological survey of HTLV-I in Mashhad, Northeastern Iran suggests an important mother to child transmission. Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 10:269.

Gessain A, Barin F, Vernant JC (1985): Antibodies to human T-lymphotrophic virus type-I in patients with tropical spastic paraparesis. Lancet 2:407–410.

Hinuma Y, Nagata K, Hanaoka M (1981): Adult T-cell leukemia: Antigen in ATL cell line and detection of antibodies to the antigen in human sera. Proceedings of the National Academy of Sciences U.S.A. 78:6476–6480.

Holmstrom A, Syrjanen S, Laine P, Valle S-L, Suni J (1990): HIV antibodies in whole saliva detected by ELISA and Western blot assays. Journal of Medical Virology 30:245–248.

Ikeda M, Fujino R, Matsui T, Yoshida T, Komoda H, Imai J (1984): A new agglutination test for serum antibodies to adult T-cell leukemia virus. Gann 75:845–848.

Kline RL, Brothers T, Halsey N, Boulos R, Lairmore MD, Quinn TC (1991): Evaluation of enzyme immunoassay antibody to human T-lymphotropic viruses type I/II. Lancet 337:30–33.

Lal RB, Brodine S, Kazura J, Mbidde-Katonga E, Yanagihara R, Roberts C (1992): Sensitivity and specificity of recombinant transmembrane glycoprotein (rgp-21)-spiked Western blot in confirming human T-lymphotropic virus types I and II infection. Journal of Clinical Microbiology 30:296–299.

Maayan S, Dan M, Marling R, Chen YM (1992): HTLV-I among Israeli intravenous drug users. International Journal of Epidemiology 5: 50–55.

Maloney EM, Biggar RJ, Neel JV, Taylor ME, Hahn BH, Shaw GM, Blattner WA (1992): Endemic human T-cell lymphotropic virus type II infection among isolated Brazilian Amerindians. Journal of Infectious Diseases 166:100–107.

Mariette X, Agbalika F, Daniel MT, Bisson M, Lagrange P, Brouet JC, Morinet F (1993): Detection of human T-lymphotropic virus type I tax gene in salivary gland epithelium from two patients with Sjögren's syndrome. Arthritis & Rheumatism 36:1423–1428.

Meytes D, Shohat B, Lee Y, Nadel G, Sidi Y, Cerney M, Swanson P, Shaklai M, Kilim Y, Elgat M, Chin E, Danon Y, Rosenblat JD (1990): Serological and molecular survey for HTLV-I infection in a high risk Middle Eastern group. Lancet 336:1533–1535.

Miller SA, Dykes DD, Polesky HF (1988): A simple salting out procedure for extracting DNA from human nucleated cells. Nucleic Acids Research 16:1215.

Miyoshi I, Sawada T, Iwahara Y, Ishii K, Kubonishi L, Taguchi H (1992): Excretion of HTLV-I in saliva. JAMA 267:236.

Neil JC, Forrest D (1987): Mechanisms of retroviruses-induced leukemia: Selected aspects. Biochimica and Biophysica Acta 907:71–91.

Nerurkar V, Achiron A, Song K, Melland R, Pinhas-Hamiel O, Melamed E, Shohat B, Yanagihara R (1995): Human T-cell lymphotropic virus type 1 in Iranian-born Mashhadi Jews: Genetic and philogenetic evidence for common source of infection. Journal of Medical Virology 45:361–366.

O'Farrel BJ, Rajan E, Albloushi SS, Courlney MG, Fielding J, Shattock AG (1997): The reliability of saliva as a sample for the detection of hepatitis A immunoglobulins under various sampling conditions. Clinical and Diagnostic Virology 7:153–157.

Osame M, Matsumoto M, Usuku K (1987): Chronic progressive myelopathy associated with elevated antibodies to human T-lymphotropic virus type I and adult T-cell leukemia like cells. Annals of Neurology 21:117–122.

Poiesz BJ, Ruscetti W, Gazdar AF, Bunn PA, Minna JD, Gallo RC (1980): Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. Proceedings of the National Academy of Sciences U.S.A. 77:7415–7419.

Riedel DA, Evans AS, Saxinger C, Blattern WA (1989): A historical study of human T-lymphotrophic virus type I transmission in Barbados. Journal of Infectious Diseases 159:603–609.

Safai B, Huang JL, Boeri E, Farid R, Raafat J, Schutzer P, Ahkami R, Franchini G (1996): Prevalence of HTLV type I infection in Iran: A serological and genetic study. AIDS Research and Human Retroviruses 12:1185–1190.

Saxinger W, Blattner WA, Levine PH (1984): Human T-cell leukemia virus (HTLV-I) antibodies in Africa. Science 225:1473–1476.

Shioiri S, Tachibana N, Okayama A, Ishihara S, Tsuda K, Essex M, Stiver S, Mueller N (1993): Analysis of anti-tax antibody of HTLV-1 carriers in an endemic area in Japan. International Journal of Cancer 53:1–4.

Shohat B, Shaklai M, Sidi Y, Nadel G, Rosenblat JD, Meytes O (1991): Elevated serum interleukin-2 receptors in a newly identified group with high rates of HTLV-I infection in Israel. Journal of Infectious Diseases 164:431–432.

Sidi Y, Meytes D, Shohat B, Fenig E, Weisbort Y, Lee Y, Pinkhas J, Rosenblat JD (1990): Adult T-cell lymphoma in Israeli patients in Iranian origin. Cancer 65:590–593.

Taylor GP (1996): The epidemiology of HTLV-I in Europe. Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 13(suppl 1):S8–S14.